

# INTERNET COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>2475/002635</b>	<b>FOR FURTHER ACTION</b> <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. <b>PCT/EP 00/05863</b>	International filing date (day/month/year) <b>23/06/2000</b>	(Earliest) Priority Date (day/month/year) <b>30/06/1999</b>
Applicant  <b>KNOLL AKTIENGESELLSCHAFT</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.  
☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

- ☐ the text is approved as submitted by the applicant.
- ☒ the text has been established by this Authority to read as follows:

**SCREENING FOR COMPOUNDS MODULATING MITOCHONDRIAL PROTON LEAK**

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- ☐ as suggested by the applicant.
- ☒ because the applicant failed to suggest a figure.
- ☐ because this figure better characterizes the invention.
- 1 ☐ None of the figures.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

## Continuation of Box I.1

Although claims 56, 58 and 60 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound.

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## Continuation of Box I.1

Claims Nos.: 56, 58, 60

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

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## Continuation of Box I.2

Present claims 53-55 relate to compounds defined by reference to a desirable characteristic or property, namely that these compounds are identifiable in a screening method according to any one of claims 3-52. Claim 56 relates to a method using these compounds and claim 57 relates to a use of these compounds.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds mentioned in the description at pages 28. lines 4-22.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 00/05863

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 G01N33/50

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data, PAJ, EMBASE, MEDLINE, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JEKABSONS M ET AL: "Effect of nucleotides on rat liver and skeletal muscle mitochondria non-phosphorylating respiration and membrane potential." FASEB JOURNAL, vol. 12, no. 5, 20 March 1998 (1998-03-20), page A813 XP002154017 Annual Meeting of the Professional Research Scientists on Experimental Biology 98, Part II; San Francisco, California, USA; April 18-22, 1998 ISSN: 0892-6638 cited in the application	1,3,5-7, 11, 15-23, 27,29-33
A	left-hand column, paragraph 4714	1-3, 34-36, 41-43, 50-52
	---	
	-/--	

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

\* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*Z\* document member of the same patent family

Date of the actual completion of the international search

3 January 2001

Date of mailing of the international search report

24/01/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Tuynman, A

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/05863

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MONEMDJOU S ET AL: "Mitochondrial proton leak in brown adipose tissue, mitochondria of UCP1-deficient mice is GDP insensitive" AMERICAN JOURNAL OF PHYSIOLOGY: ENDOCRINOLOGY AND METABOLISM, June 1999 (1999-06), pages E1073-E1082, XP002154018 abstract page E1074, left-hand column, line 7 -page E1075, left-hand column, line 42 page E1075; figure 1 page E1076; figure 3	1,3,6,7, 10,11, 14-23, 25-28, 30,31,33
A	---	1,3,36, 41,43, 50,52
A	EARNSHAW M J ET AL: "THE ADENINE NUCLEOTIDE CARRIER OF PLANT MITOCHONDRIA CONTRACTION INDUCED BY ADP" PLANT SCIENCE LETTERS, vol. 6, no. 5, 1976, pages 343-348, XP000972265 ISSN: 0304-4211 the whole document	1-4,21, 34
A	BOUILLAUD F ET AL: "A sequence related to a DNA recognition element is essential for the inhibition by nucleotides of proton transport through the mitochondrial uncoupling protein." EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 13, no. 8, 1994, pages 1990-1997, XP002154020 ISSN: 0261-4189 abstract page 1994; figure 7	1-4,7,9, 11,13, 29,32, 34,35, 41,42, 50,51
X	BLOCK M R ET AL: "INTERACTION OF 3'-O-1 NAPHTHOYL ADP A FLUORESCENT ADP ANALOG WITH THE ADP ATP CARRIER PROTEIN IN THE MITOCHONDRIAL MEMBRANE" BIOCHEMISTRY, vol. 21, no. 22, 1982, pages 5451-5457, XP002154021 ISSN: 0006-2960 abstract	37-40
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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/05863

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	CADENAS S ET AL: "AMP decreases the efficiency of skeletal-muscle mitochondria" BIOCHEMICAL JOURNAL, vol. 351, no. 2, 15 October 2000 (2000-10-15), pages 307-311, XP000974944 the whole document	1-52
X	PARES, XAVIER ET AL: "The reaction of bovine pancreatic ribonuclease A with 6-chloropurineriboside 5'- monophosphate. Evidence on the existence of a phosphate-binding sub-site" EUR. J. BIOCHEM. , vol. 105, no. 3, 1980, pages 571-580, XP000974761	53-55
A	abstract	57, 59

**PCT**

**NOTIFICATION OF THE RECORDING  
 OF A CHANGE**

(PCT Rule 92bis.1 and  
 Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

NASH, David, Allan  
 Haseltine Lake & Co.  
 Imperial House  
 15-19 Kingsway  
 London WC2B 6UD  
 ROYAUME-UNI

<b>Date of mailing</b> (day/month/year) 13 December 2001 (13.12.01)	<b>IMPORTANT NOTIFICATION</b>
<b>Applicant's or agent's file reference</b> 2475/002635	
<b>International application No.</b> PCT/EP00/05863	<b>International filing date</b> (day/month/year) 23 June 2000 (23.06.00)

1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

<b>Name and Address</b> KNOLL AKTIENGESELLSCHAFT D-67061 Ludwigshafen Germany	<b>State of Nationality</b> DE	<b>State of Residence</b> DE
	<b>Telephone No.</b>	
	<b>Facsimile No.</b>	
	<b>Teleprinter No.</b>	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☒ the name ☐ the address ☐ the nationality ☐ the residence

<b>Name and Address</b> KNOLL GMBH D-67061 Ludwigshafen Germany	<b>State of Nationality</b> DE	<b>State of Residence</b> DE
	<b>Telephone No.</b>	
	<b>Facsimile No.</b>	
	<b>Teleprinter No.</b>	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned  
☐ the International Searching Authority ☒ the elected Offices concerned  
☐ the International Preliminary Examining Authority ☐ other:

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	<b>Authorized officer</b>  Ki-Nam HA  Telephone No.: (41-22) 338.83.38
--	--

**PCT**

**NOTIFICATION OF THE RECORDING  
 OF A CHANGE**

(PCT Rule 92bis.1 and  
 Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

GOLDSCHIED, Bettina  
 BASF Aktiengesellschaft  
 D-67056 Ludwigshafen  
 ALLEMAGNE

<b>Date of mailing</b> (day/month/year) 07 November 2001 (07.11.01)	<b>IMPORTANT NOTIFICATION</b>
<b>Applicant's or agent's file reference</b> 2475/002635	
<b>International application No.</b> PCT/EP00/05863	<b>International filing date</b> (day/month/year) 23 June 2000 (23.06.00)

1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

<b>Name and Address</b> KNOLL AKTIENGESELLSCHAFT	<b>State of Nationality</b> DE	<b>State of Residence</b> DE
	<b>Telephone No.</b>	
	<b>Facsimile No.</b>	
	<b>Teleprinter No.</b>	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☒ the name ☐ the address ☐ the nationality ☐ the residence

<b>Name and Address</b> KNOLL GMBH	<b>State of Nationality</b> DE	<b>State of Residence</b> DE
	<b>Telephone No.</b>	
	<b>Facsimile No.</b>	
	<b>Teleprinter No.</b>	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned  
☐ the International Searching Authority ☒ the elected Offices concerned  
☐ the International Preliminary Examining Authority ☐ other:

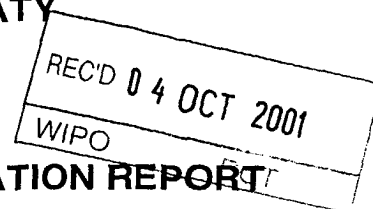
<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland	<b>Authorized officer</b> Ki-Nam HA
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference 2475/002635		<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP00/05863	International filing date (day/month/year) 23/06/2000	Priority date (day/month/year) 30/06/1999	
International Patent Classification (IPC) or national classification and IPC C12Q1/00			
Applicant KNOLL AKTIENGESELLSCHAFT et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  08/12/2000	Date of completion of this report  01.10.2001
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Hinchliffe, P  Telephone No. +49 89 2399 8431  



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/05863

## I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

### Description, pages:

1-29 as originally filed

### Claims, No.:

1-60 as originally filed

### Drawings, sheets:

1/1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/05863

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

## III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.  
☒ claims Nos. 1,2,34-36,41-43,47-60.

because:

- ☒ the said international application, or the said claims Nos. 55,56,58,60 (with respect to I.A.) relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1,2 are so unclear that no meaningful opinion could be formed (*specify*):  
**see separate sheet**
- ☒ the claims, or said claims Nos. 34-36,41-43,47-60 are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.  
☐ the computer readable form has not been furnished or does not comply with the standard.

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/05863

	No:	Claims	3,5-7,9-11,13-23,25-33,37-40,44-46
Inventive step (IS)	Yes:	Claims	
	No:	Claims	3,4,5-7,8,9-11,12,13-23,24,25-33,37-40,44-46
Industrial applicability (IA)	Yes:	Claims	3-33,37-40,44-46
	No:	Claims	

2. Citations and explanations  
**see separate sheet**

## VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:  
**see separate sheet**

## VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/EP00/05863

**ITEM III**

1. In contrast to the ISR, the IPEA is of the opinion that claims 1 and 2 are so unclear that a meaningful examination is not possible (see item VIII below for the reasons).
2. Claims 55,56,58,60 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

**ITEM V**

1. Claims 3,5-7,9-11,13-23,27,29-30 are not novel, contrary to Article 33(2) PCT, in the light of D1 (as cited sequentially in the ISR). This document discloses a method of testing the effects of nucleotides on non-phosphorylating  $VO_2$  which involves the steps covered by the said claims.
2. Claims 3,6,7,10,11,14-23,25-28,30-33 are also not novel, contrary to Article 33(2) PCT, in the light of D2 (as cited sequentially in the ISR). Again this document discloses methods whereby the effects of nucleotides on UCPs is measured using an oxygen electrode (see in particular materials and methods section).
3. Claims 37-40, are not novel, contrary to Article 33(2) PCT, in the light of D5 (as cited in the ISR). This document discloses that a mitochondrial transporter protein (ANC is apparently a member of this family and is responsible for shuttling ADP/ATP) may be inhibited by N-ADP, a fluorescently labelled analog of ADP. In addition CATR and bongkreikic acid are both compounds that reduce the amount of the labelled ligand (see in particular p.5453, col.1, fourth paragraph).
4. Claims 4,8,12,24 do not involve an inventive step contrary to Article 33(3) PCT. The particular modifications made to the assays of either D1 or D2 are considered to be routine and within the realms of a normally skilled person.
5. Claims 44-46 are not novel (Article 33(2) PCT) in the light of D2. It is assumed

that the UCP 1-3 proteins of this document are equivalent to the ANC 1-3 proteins mentioned on page 13, line 21 of the description. This document teaches an assay whereby GDP was used to control non phosphorylative oxidation in mice lacking UCP-1. Comparison with normal systems showed that UCP-2 and UCP-3 were not GDP sensitive. Consequently D2 discloses an assay for identifying compounds which modulate proton leak.

6. For the assessment of the present claims 55,58,60 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

#### **ITEM VII**

1. Contrary to the requirements of Article 5 PCT, claims 34-36 and 41-43,47-60 are not supported by the description. It is only assumed that the compounds identified will have an effect on obesity (see p.2, lines 13-15 and p.28, lines 24-31). No actual evidence is provided to substantiate any of the claims and consequently the claims do not fulfill the requirements of said Article. The same is true for cachexia. In addition the introduction of D2 notes that UCP-1 deficient mice were not obese as expected, leading to further doubts as to whether the currently identified compounds/methods would really be useful for treating obesity.

#### **ITEM VIII**

1. Claims 1 and 2 are deemed to be contrary to the requirements of Article 6 PCT because they are unclear insofar as they fail to provide sufficient information for any valid opinion to be formed on whether they are novel or inventive. For instance the prior art document D1 (as cited in the ISR) discloses several proteins related to UCP-1 which are involved in non phosphorylating respiration. Any of these proteins could be or include such a site, but as the claims fail to mention whether protein or gene regulation is occurring the skilled person is left completely

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/EP00/05863

confused as to what sort of regulatory site is encompassed.

2. The term "ANC", found in claims 34 et seq. should be clarified on its first use (Article 6 PCT).

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 00/05863

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/50

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data, PAJ, EMBASE, MEDLINE, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JEKABSONS M ET AL: "Effect of nucleotides on rat liver and skeletal muscle mitochondria non-phosphorylating respiration and membrane potential." FASEB JOURNAL, vol. 12, no. 5, 20 March 1998 (1998-03-20), page A813 XP002154017 Annual Meeting of the Professional Research Scientists on Experimental Biology 98, Part II; San Francisco, California, USA; April 18-22, 1998 ISSN: 0892-6638 cited in the application	1,3,5-7, 11, 15-23, 27,29-33
A	left-hand column, paragraph 4714	1-3, 34-36, 41-43, 50-52
	--- -/--	

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

\* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\* & \* document member of the same patent family

Date of the actual completion of the international search

3 January 2001

Date of mailing of the international search report

24/01/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Tuynman, A

## INTERNATIONAL SEARCH REPORT

Inter:      nal Application No

PCT/EP 00/05863

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>MONEMDJOU S ET AL: "Mitochondrial proton leak in brown adipose tissue, mitochondria of UCP1-deficient mice is GDP insensitive" AMERICAN JOURNAL OF PHYSIOLOGY: ENDOCRINOLOGY AND METABOLISM, June 1999 (1999-06), pages E1073-E1082, XP002154018— abstract page E1074, left-hand column, line 7 -page E1075, left-hand column, line 42 page E1075; figure 1 page E1076; figure 3</p>	<p>1,3,6,7, 10,11, 14-23, 25-28, 30,31,33</p>
A		<p>1,3,36, 41,43, 50,52</p>
A	<p>--- EARNSHAW M J ET AL: "THE ADENINE NUCLEOTIDE CARRIER OF PLANT MITOCHONDRIA CONTRACTION INDUCED BY ADP" PLANT SCIENCE LETTERS, vol. 6, no. 5, 1976, pages 343-348, XP000972265 ISSN: 0304-4211 the whole document</p>	<p>1-4,21, 34</p>
A	<p>--- BOUILLAUD F ET AL: "A sequence related to a DNA recognition element is essential for the inhibition by nucleotides of proton transport through the mitochondrial uncoupling protein." EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 13, no. 8, 1994, pages 1990-1997, XP002154020 ISSN: 0261-4189 abstract page 1994; figure 7</p>	<p>1-4,7,9, 11,13, 29,32, 34,35, 41,42, 50,51</p>
X	<p>--- BLOCK M R ET AL: "INTERACTION OF 3'-O-1 NAPHTHOYL ADP A FLUORESCENT ADP ANALOG WITH THE ADP ATP CARRIER PROTEIN IN THE MITOCHONDRIAL MEMBRANE" BIOCHEMISTRY, vol. 21, no. 22, 1982, pages 5451-5457, XP002154021 ISSN: 0006-2960 abstract</p>	<p>37-40</p>
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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 00/05863

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	CADENAS S ET AL: "AMP decreases the efficiency of skeletal-muscle mitochondria" BIOCHEMICAL JOURNAL, vol. 351, no. 2, 15 October 2000 (2000-10-15), pages 307-311, XP000974944 the whole document	1-52
X	PARES, XAVIER ET AL: "The reaction of bovine pancreatic ribonuclease A with 6-chloropurineriboside 5'- monophosphate. Evidence on the existence of a phosphate-binding sub-site" EUR. J. BIOCHEM. , vol. 105, no. 3, 1980, pages 571-580, XP000974761	53-55
A	abstract	57, 59

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.1

Although claims 56,58 and 60 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound.

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## Continuation of Box I.1

Claims Nos.: 56,58,60

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

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## Continuation of Box I.2

Present claims 53-55 relate to compounds defined by reference to a desirable characteristic or property, namely that these compounds are identifiable in a screening method according to any one of claims 3-52. Claim 56 relates to a method using these compounds and claim 57 relates to a use of these compounds.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds mentioned in the description at pages 28. lines 4-22.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.